Economic Evaluations in Pain Management: Principles and Methods

Carl V. Asche
Brian Seal
Kenneth C. Jackson, II
Gary M. Oderda

ABSTRACT. This paper describes how investigators may design, conduct, and report economic evaluations of pharmacotherapy for pain and symptom management. Because economic evaluation of therapeutic interventions is becoming increasingly important, there is a need for guidance on how economic evaluations can be optimally conducted. The steps required to conduct an economic evaluation are described to provide this guidance. Economic evaluations require two or more therapeutic interventions to be compared in relation to costs and effects. There are five types of economic evaluations, based on analysis of: (1) cost-effectiveness, (2) cost-utility, (3) cost-minimization, (4) cost-consequence, and (5) cost-benefit analyses. The six required steps are: identify the perspective of the study; identify the alternatives that will be compared; identify the relevant costs and effects; determine how to collect the cost and effect data; determine how to perform calculation for cost and effects data; and determine the manner in which to depict the results and draw comparisons. *[Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <http://www.HaworthPress.com>*

KEYWORDS. Pain, economics, cost-benefit, statistics, research, health services, randomized controlled trials, methods, design, sensitivity, specificity

BACKGROUND AND HISTORY

Recent history has seen great increases in expenditures and rises in healthcare services. The 1950s and 1960s were a period of massive expansion in the number of healthcare facilities, schools and training programs, and advances in healthcare technology. Concurrently there was an increase in the number of Americans being insured because of the implementation of Medicare and Medicaid.

The cost of healthcare increased in the 1970s and 1980s as a result of fee-for-service payment structure and growth in healthcare service utilization. Private insurers, most notably Blue Cross and Blue Shield plans, also increased through employers for hospital and physician services. The rise in healthcare spending rose

Carl V. Asche, PhD, is Research Associate Professor, Pharmacotherapy Outcomes Research Center (PORC), Department of Pharmacotherapy, University of Utah College of Pharmacy; Brian Seal, RPh, MBA, PhD, is Adjunct Assistant Professor of Pharmaceutical Business, University of the Sciences in Philadelphia, 600 South 43rd Street, Philadelphia, PA 19104-4495; Kenneth C. Jackson, II, PharmD, is Clinical Associate Professor of Pharmacotherapy, PORC; Gary M. Oderda, PharmD, MPH, is Professor and Director, PORC.

Address correspondence to: Carl V. Asche, PhD, Pharmacotherapy Outcomes Research Center, 421 Wakara Way, Salty Lake City, UT 84108 (E-mail: carl.asche@pharm.utah.edu).

Journal of Pain & Palliative Care Pharmacotherapy, Vol. 20(3) 2006
Available online at http://www.haworthpress.com/web/JPPCP

doi:10.1300/J354v20n03_04

from four to 11 percent of the Gross National Product (GNP).

Due to continually increasing in healthcare costs in the 1980s and 1990s, healthcare payers increasingly questioned the value of these services. Documented evidence demonstrated a wide range in the quality of care differences across geographical regions, motivating researchers and policy-makers to take a closer look at healthcare delivery. Concurrently managed care came into being using risk-sharing and cost-cutting measures such as the prospective payment to contain healthcare costs. A prospective payment system through which governmental programs pay predetermined fixed amounts was added by Medicare in the 1980s and managed care soon followed, but the gatekeeper concept introduced in the 1990s was the true cost savers in response to increase in pharmacy benefit manager (PBM) coverage.

Rising Pharmaceutical Costs

Pharmaceuticals are one small contributor to growing healthcare costs, but drugs have seen the greatest increases in expenditures compared to other healthcare services. For example, Medical expenditures were growing at rates of six, nine, and 12 percent in 1998, 1999, and 2000, respectively, whereas pharmaceutical expenses increased 15 to 16 percent, during the same time period. These dramatic increases in pharmaceutical spending can be attributed to greater cost of new drugs coming into the market and the greater volume of overall drug utilization due to better prescription insurance and changing demographics.

Assessing the Value of Pharmaceuticals

Traditionally, before decision makers will pay for pharmacotherapy they must be convinced of its efficacy, i.e., the drug has to be seen as being able to work in optimal conditions. After evidence of efficacy has been established, the next type of evidence that healthcare decision makers seek is that which demonstrates that the drug is effective in the usual-care settings including resource constraints, compliance issues, and a broader cross-sections of patients.

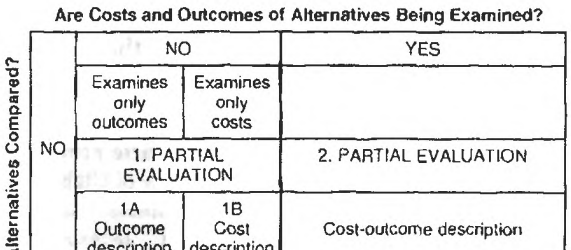
As a result of the dramatic spending increases for pharmaceuticals, decision makers now increasingly question whether new and expensive drugs are worth what they cost. For example, new long-acting oral opioid formulations have been introduced with evidence that they may offer benefits over currently available long-acting opioids for some patients due to the new dosage forms allowing once daily dosing and better patient adherence. But the new agents typically cost considerably more than the older agents in this class. Payers therefore question whether the sustained action of the newer dosage forms is worth the higher price. Properly designed pharmacoeconomic analyses are needed to answer this type of question.

Types of Healthcare Evaluations

There is a variety of types of healthcare evaluations. In general, as depicted in Figure 1, one can classify these evaluations into two groups. The first row in the figure applies when only one medical service or drug is being evaluated and the second row when more than one alternative is being examined. As represented by the columns, one can perform evaluations of only costs, only outcomes, or both costs and outcomes. A full economic evaluation involves at least two alternatives being compared and evaluated for both costs and outcomes.

Pharmacoeconomics, by definition, should provide full economic evaluation. However, some published studies incorrectly claim to be pharmacoeconomic analyses when those eval-

FIGURE 1. Types of Healthcare Evaluations



uations actually fall into one of the partial evaluation boxes.

WHEN IS A FORMAL ANALYSIS NEEDED?

Formal analyses are not always needed. Before conducting any economic analysis of a healthcare technology, program, or service, the investigator must first determine whether the analysis is needed. For example, as depicted in the Figure 2, if the cost of a new drug is lower and the drug is more effective than current therapy, or vice-versa, no pharmacoeconomic analysis is indicated. The choice of therapy is obvious as represented by the lower left and upper right boxes in Figure 2. If comparator therapies have the same efficacy or effectiveness and same price, then the choice is based on the decision makers' preferences; no economic analysis is required to assist in decision making. However, when a new drug has higher effectiveness than existing therapy and costs more, or vice-versa, a formal economic analysis is warranted.

WHAT IS PHARMACOECONOMICS?

Pharmacoeconomics is a decision-assisting tool which evaluates healthcare resources consumed to produce health and economic outcomes. Valuation of resources and outcomes follows a three-step process:

- identify the relevant resources and outcomes,
- measure resources and outcomes using appropriate physical units, and
- compare them.

FIGURE 2. Requirements for a Formal Economic Analysis

EFFECT	COST (of drug relative to the alternative)		
	Higher	Equal	Lower
Higher	Yes	No	No
Equal	No	No	No
Lower	No	No	Yes

Problems may be encountered in all three phases. Some items are difficult to identify in health care interventions.

Not all resources and outcomes can be measured in appropriate physical units. For example, some interventions have subjective outcomes such as the reduction of pain or increase in one's quality of life. The identification and measurement of these resources and outcomes depend on the perspective of the study and time frame used.

Perspective and Time

The perspective of the study defines the viewpoint form which the study is undertaken.[1] A pharmacoeconomic analysis can be conducted from several perspectives, e.g., that of the provider, payer, patient or society. The study perspective should be clearly stated because the perspective determines the relevance of costs and outcomes that need to be identified and valued. Study results will widely vary depending on the perspective of the study. For example, if you are considering a payer's (such as the health plan) perspective, then resources and outcomes relevant to the health plan would be identified, measured, and compared. Resources may include services for which the health plan pays for, e.g., prescriptions, office visits, lab tests. The health plan would be less concerned about how soon the patients feel better enabling them to return to work, while that consideration would be of direct relevance to the patients' employers, i.e., it would be their perspective

Similarly the time period over which a product or service is evaluated is also important and depends on the epidemiological or clinical evidence of the healthcare services being evaluated. An example of a short-term time frame analysis is the cost of using epidural analgesia in the postoperative period to manage pain associated with orthopedic procedures. Another example could be use of serotonin 5-HT-1 antagonists (triptans) to abort migraine headaches. A long-term time frame may be more relevant when one is evaluating preventive services with which costs of the program may occur now but benefits or health outcomes attributable to the intervention may be seen only in the near or distant future. An example of this longer time frame would be use of interdisci-

plinary care in managing patients with chronic nonmalignant pain. In this setting, a patient may not present with maximal improvement until some distant time. It is possible for major benefits associated with the cost of type of care to occur after conclusion of interdisciplinary care. Thus depending on the clinical relevance and the time availability data, the measurement of resources and outcomes may vary according to the time of the study chosen.

VALUATION/MEASUREMENT OF RESOURCES

Resources

Resources are always valued in terms of costs. Theoretically, economists consider these costs to be the benefits of opportunities foregone (opportunity cost). Because opportunity costs are difficult to infer, researchers often use reference prices or reimbursement rates to value resources. Reference prices are list prices that serve as references for particular products or services, whereas reimbursement rates are the actual costs of a services or goods. Costs can be divided into four categories: direct medical costs; direct non-medical costs; indirect costs; and intangible costs.

1. Direct medical costs are costs of medical resources consumed that are directly related to the medical product or service being evaluated. For example, copay amount for a physician visit or out-of-pocket expenses when patients purchase prescription medications.
2. Direct non-medical costs are costs of non-medical resources consumed as the result of providing or obtaining the medical goods or services under evaluation. For example, transportation costs to go and see your doctor.
3. Indirect costs are costs "indirectly" associated with the consumption of a medical product or service under evaluation. For example, people who are sick either don't show up at work (absenteeism) or work at a lesser efficiency (presenteeism). From an employer's perspective the costs associated with lost productivity would be considered as an example of indirect cost.
4. Intangible costs are defined as costs associated with pain and suffering resulting from a treatment or illness itself. There is some debate among economists as to whether to include these as costs or value them as outcomes.

Examples of Data Sources to Measure Resources

Values for resource information can come from various sources and should always be valid and relevant to the pharmacoeconomic study under consideration. Table 1 lists some sources of reference prices or reimbursement rates. Rather than go into detail as to the various advantages and disadvantages of these data sources, it is sufficient to say that none of these is perfect; some are very close to the true cost of the medical service or drug and some a bit farther away. Each data source comes with a time, and money constraint.

Valuation/Measurement of Outcomes

When identifying health or economic outcomes, one can chose from a list of outcomes. Broadly these outcomes are classified into three categories, i.e., economic, clinical, and humanistic outcomes.

1. Economic outcomes are usually valued in terms of costs or resource use of services or goods avoided due to a treatment. For example if an investigator wishes to compare sumatriptan and almotriptan for migraine headache management, a potential economic outcome could be the number of urgent visits or hospitalizations that persons taking the drugs experienced due to chest pain, a common adverse event of triptans. The drug with the lower incidence of this adverse outcome would be considered superior in terms of an outcome evaluation.
2. Clinical outcomes include those that are generally reported in a clinical trial or real-world clinical studies and may include the efficacy/effectiveness of a drug. These are the easiest to measure

with the simplest being mortality. Clinical outcomes may include clinical efficacy/effectiveness, relief or reduction in symptoms.

3. Humanistic outcomes include patient compliance and quality of life. These are the most difficult to measure. However, in chronic pain management and palliative care, humanistic outcomes are very important.

When shifting from quantitative to qualitative outcomes, measurement becomes a challenge. It is also a challenge to identify the most relevant and desirable outcomes when comparing therapies.

Returning to the earlier example of interdisciplinary chronic nonmalignant pain management, what types of qualitative measures should be considered? In chronic nonmalignant pain it is necessary to consider the patient's report of pain intensity, psychological state, perceived and real functional ability, and overall enjoyment of life. One method to achieve this assessment is use of the Treatment Outcomes in Pain Survey (TOPS).[2,3] This fully validated, chronic pain-specific health-related quality of life instrument provides for measuring pain-related outcomes, across fourteen scales as depicted in Table 2. The sixty-item TOPS questionnaire includes the full Medical Outcomes Study Short Form 36 (SF-36) and captures additional data on pain, functional limitations, perceived and real family/social disability, and formal work disability. A unique feature of the TOPS is that it can be used to measure individual patients HRQoL over time, as well as serving as a useful research tool.[4]

Both careful examination and a good knowledge of the clinical epidemiology of the therapies under study are essential in addition to the kinds of data that are available. It is usually easier to find data on short-term outcomes and harder for long term outcomes.

The overall goal of any pharmaceutical intervention is theoretically to influence the long term outcomes such as decreased morbidity and prolongation of life. Therefore, if one includes only short term health outcomes due to time constraints one needs to assure that the short term outcomes correlate well with the long term outcomes.

HEALTH RELATED QUALITY OF LIFE (HRQOL)

When you do "something" to a human being, it may impact his/her health, especially if that "something" is a treatment. Before attempting to measure the impact of disease or therapy on health or changes in health, one must address the question of defining health.

According to the 1948 World Health Organization definition, health is a state of complete physical, mental, and social well-being, and not merely the absence of disease or infirmity.[5] With such a broad definition, measurement of health has traditionally focused on the latter part of the definition, i.e., the absence of disease. This is evident by the emphasis and importance of use of objective clinical patient outcomes such as laboratory values within the medical community.

TABLE 1. Types of Resources

Sources	Examples
Physician Fee Schedules	Medicare Fee Schedule
Hospital Charges	Hospital Claims Database
Insurance/Employer Claims	State Medicaid; MedStat MarketScan Database
Average Whole-Sale Price (AWP) or Wholesale Acquisition Cost (WAC) for Drugs	Red Book or claims from a PBM
Electronic Medical Records	Veterans Health Administration's Decision Support System (DSS)
National Surveys	Medical Expenditure Panel Survey (MEPS)

TABLE 2. Treatment Outcomes in Pain Survey (TOPS) Scales

Pain Symptom	Objective Work Disability
Work Limitations	Lower Body Functional Limitations
Upper Body Functional Limitations	Perceived Family/Social Limitations
Objective Family/Social Limitations	Total Pain Experience
Life Control	Passive Coping
Solicitous Response	Fear Avoidance
Satisfaction with Outcomes	Healthcare Satisfaction

The term 'health-related quality of life' (HRQoL) is often applied to the impact of disease and treatment on patients' lives. It is disease-specific whereas quality of life (QoL) is a concept which encompasses an individual's perceived level of physical, psychological, and social well-being. HRQoL aims to encompass the entire construct of health and is defined as a person's or a group's subjective assessment of their functioning and well-being. For that reason it is gaining great popularity as an outcome measure within the medical community. This popularity is evident with the increase in number of publications in the literature in the past two decades.

In 1973 only five articles listed "quality of life" as a reference keyword in the MEDLINE database; this number grew to 16,256 in 1998. Quality of life is now recognized as important in the management of chronic diseases and is widely monitored in chronically ill patients. It has also been used in evaluating treatment in clinical trials, as well as in allocating resources at the health policy levels.

Measuring HRQOL

Typically, HRQoL measurement is done through psychometrically validated questionnaires which are designed to assess patients' perception of their illness, and its impact on their lives. Measurement of HRQoL usually encompasses three major domains.

1. Physical well-being (or status) which measures how an illness or your current health impact the individual's activities of daily living, e.g., using the bathroom, climbing stairs.
2. Social/role functioning is the domain which measures how one's health or illness impacts his/her ability to interact with others.
3. Emotional/psychological well-being or status measures the impact on mental health, e.g., questions about how stressed or nervous the subject has been, whether s/he has felt downhearted, and quantitates this construct.

A few HRQoL instruments also measure disease- or treatment-related symptoms. There are two types of HRQoL measures–generic or disease-specific.

1. General measures (e.g., the Medical Outcomes Study [MOS] Short Form 36, SF-36) applicable across all diseases, medical interventions, and a wide variety of populations.
2. Disease-Specific measures (e.g., Asthma Quality of Life Questionnaire) applicable for specific conditions or diagnoses.

These measures come in two formats, i.e., profiles which are descriptive in nature and indices which measure utility.

1. Health profile HRQoL measures represent independent dimension scores that are important and relevant to clinicians who would like to assess the effect of a therapy on various dimensions of a patient's HRQoL and thus better guiding patient care. An example of health profile is the SF-36 which is represented by an array of scores for individual quality of life or health status dimensions.
   a. The advantage is that the health profile provides an outcome score for individual dimensions to allow for determination of differential effect.
   b. The disadvantage is that one cannot aggregate across all dimensions for a composite or unitary measure of health status or quality of life.
2. A Health Index (e.g., Quality of well being scale, Health utility index, EuroQol 5 Dimensional Format) is a single, overall score ranging from zero to one, representing the quality of life associated with death and perfect health, respectively.
   a. The advantage is that index scores can be used in more in-depth outcome assessment (e.g., Cost Utility Analysis)
   b. The disadvantage is that it usually does not provide scores for individual dimensions.

DISCOUNTING

Inputs and consequences of a health intervention accrue at different times, especially for

chronic disease and population-based programs developed to deal with them. In such a case one cannot directly compare the inputs of a program starting today with its consequences which will accrue in thirty years' time.

Economists adjust the valuation of such consequences to take account of the difference in time by using a technique called discounting which allows the calculation of the present values of inputs and benefits which accrue in the future.

Discounting is primarily based on selection of a preferred time, e.g., individuals prefer to forego a part of the benefits/payment if they accrue it now, rather than fully in the uncertain future. The strength of this preference is expressed by the discount rate which is inserted in economic evaluations. The choice of a discount rate and the choice of which items it should be applied to are a matter of intense debate among economists.

Some examples used are bank interest or mortgage rates; inflation rate (e.g., Medical Consumer Price Index); or standard discount rate used in economic literature are used to calculate present values.

SENSITIVITY ANALYSIS (SA)

Parameters that go into a pharmacoeconomic model are usually estimates of the true costs of outcomes. To deal with this uncertainty, pharmacoeconomic evaluations use a technique called sensitivity analysis which repeats the comparison of alternatives by varying the estimates within a certain range to determine how it would influence the end results.

Caution is needed when conducting a sensitivity analysis (SA) because estimates may be guesses or may be associated with expert opinions or anecdotal evidence. There are areas of methodological controversy (e.g., discount rates) and one has to be careful when generalizing to other settings (e.g., demographic differences).

There a number of different types of SA which include:

1. One way SA or threshold analysis whereby, for example, only one parameter at a time is changed, holding everything else constant to determine the influence on the end results.
2. Multi-way SA or threshold analysis whereby two or more parameters are varied simultaneously.
3. Probabilistic analyses are a type of SA in which the probability of an uncertain parameter is varied within the specified distribution of the uncertain parameter.

OVERVIEW OF PHARMACOECONOMIC METHODOLOGIES

By definition pharmacoeconomic analyses are simply resource-outcome analysis. Resources are valued in terms of costs, and outcomes or consequences of drug therapy are either valued in terms of natural units or monetary units. There are five general types of pharmacoeconomic analyses as described below.

Cost-Minimization Analysis

Cost-Minimization Analysis (CMA) values resources as costs and outcomes are assumed to be identical. The goal of CMA is to identify the least expensive alternative. Results of a CMA analysis are expressed in monetary units, as only resources between the alternatives are compared. Theoretically, since no two interventions have the same exact clinical outcomes, CMA is seldom used. However, there are some situations like comparisons of brand and generic versions of the same product, or comparisons of different routes of administration of the same drug, where CMA could be applied.

Cost-Effectiveness Analysis

Cost-Effectiveness Analysis (CEA) is the most widely used pharmacoeconomic method. Here resources are valued in monetary units. Outcomes are valued in natural units such as years of life saved, symptom free days, percent low density lipoprotein (LDL) reduction. Therefore results are expressed as cost per natural unit. In CEA alternatives that can be expressed in the same natural units are compared. Consider two anticonvulsants used to treat neuro-

pathic pain. Both drugs may provide an average 30% decrease in patient-reported pain and have very similar adverse effect profiles. In this example drug A is available generically and at half the cost of the brand name only drug B product. Since both drugs have the same outcome (i.e., 30% pain reduction) drug A is more cost-effective. However consider the situation where there is a difference in pain reduction between these drugs. For example, drug A decreases pain report by 25% and drug by 35%. Since the outcome has changed, it is not possible to conduct a cost effectiveness analysis. A similar dilemma occurs when one considers costs associated with adverse events and these costs differ between two therapies. In this situation a cost-effectiveness analysis would be inappropriate. The CEA can be presented as an average CE ratio via a formula,(the cost of therapy/outcome measured in natural units), incremental CE ratio, and what the additional amount would need to be paid to obtain the additional effect. Advantages of a CEA is that it serves to compare varied forms of therapy (e.g., different classes of drugs to treat the same disease), physicians and payers find it useful and acceptable, and Intermediaries (short-term outcomes) can be evaluated. A disadvantage is that alternatives must have similar outcomes.

Cost-Utility Analysis

Cost-Utility Analysis (CUA) by definition is a form of CEA in which outcomes are adjusted for patient preferences (utility). Utility is a concept used by economists to measure satisfaction or well-being and it forms the basis for many models of consumer choice. Consumers will purchase goods that give them the greatest utility per dollar spent. Cost-utility analysis attempts to measure the utility derived from changes in health status and to calculate the cost per unit of utility. The goal is to determine which alternative accomplishes the given objective at the least cost. In pharmacoeconomic evaluations, the most common measure of utility is the quality adjusted life year, pronounced as QALY. QALY: a unit of outcome in which the quantity of life (i.e., survival) is adjusted for its quality (i.e., functioning and well-being). This complicated method developed to: overcome the limitations of a CEA methodology where comparisons of therapies had to be limited to similar outcomes; and to compare interventions that affect not only mortality (i.e., quantity of life) but also morbidity (quality of life)–a classic example would be palliative chemotherapy for terminally ill cancer patients. In this setting, one considers the cost of providing palliative chemotherapy in terms of what this provides to lengthen life and what quality of life is provided from this intervention.

Cost-Benefit Analysis

Cost-Benefit Analysis (CBA) compares resources and outcomes of a program or treatment measured in monetary terms. The characteristics of CBA allow it to compare alternatives with similar and dissimilar outcomes, resources and outcomes measured in monetary units, and results reported as net benefits (B-C) and benefit to cost ratio (B/C). The objective of a CBA is to find the alternative with the greatest net benefit; determine whether a good or service has a positive net benefit. An advantages of CBA is that it can compare wide-varying programs and services, is easily understood. A disadvantages of CBA is that the valuation of outcomes in monetary terms can be challenging and that it is not widely excepted in healthcare environment.

Cost-Consequence Analysis

Cost-Consequence Analysis (CCA) is a presentation of all costs (direct, indirect) and all outcomes (clinical, humanistic, and economic) in a tabular form without aggregating it into any form of cost-outcome ratio. The characteristics of CCA is that resources are measured in monetary units, outcomes are measured in multiple ways, and results are presented in a tabular format. The objective of CCA is to assist decision makers for choosing the most relevant resource-outcome ratio. An advantage of CCA is that it is transparent, flexible, conceptually the simplest, avoids controversies, and is the most comprehensive. A disadvantages of CCA is that it is labor/resource intensive.

Table 3 summarizes the pharmacoeconomic methodologies discussed in this section.

TABLE 3. Summary of Pharmacoeconomic Methods

Type of PE Analysis	Resources	Outcomes
Cost-minimization	Monetary units	Natural units
Cost-effectiveness	Monetary units	Natural units
Cost-utility	Monetary units	Quality-Adjusted Life Years
Cost-benefit	Monetary units	Monetary units
Cost-consequence	Monetary units	All of the above

GENERAL STEPS IN DESIGNING A PHARMACOECONOMIC STUDY

After determining that a formal economic evaluation is necessary, the investigator should complete the following seven steps to design and conduct the study.

1. Define the problem (e.g., what is a cost-effective way of managing hypertension in a defined population?). Defining the problem will help you determine the appropriate pharmacoeconomic methodology that you will need to use.
2. Identify alternative interventions (e.g., pharmaceutical) which may include drug therapy with ACE-inhibitors, and calcium channel blockers, life-style interventions may include diet and exercise.
3. Identify the perspective in terms of whose view-point needs to be considered for this study.
4. Identify and measure relevant resources and outcomes.
5. Discount costs and outcomes if they need to be.
6. Conduct a sensitivity analysis to over a range of estimates that you have assumed or measured to determine whether they are robust, meaning do they change the study results if you vary them.
7. Report the pharmacoeconomic results.

SUMMARY

Due to the growing healthcare costs, decision-makers in the healthcare market are becoming increasingly cost-conscious and increasingly question the costs and value of healthcare interventions. Pharmacoeconomics evolved from such cost and value concerns and is an important tool that can assist decision-makers in optimizing healthcare resources. Pharmacoeconomic analyses are indicated only when both cost and effect of the alternative therapy are higher or lower than standard treatment. There is always the challenge to identify and assign value to relevant resources. This includes both direct and indirect costs of economic, clinical and humanistic outcomes.

HRQoL is now accepted as an important type of outcome in addition to clinical outcomes, especially in chronic disease conditions. It is also becoming a routine component to assess quality of health care.

Discounting costs and outcomes to a present day value are important especially if they are accrued over several years.

Investigators should perform sensitivity analyses to understand how changes in the model inputs influence the outputs.

And finally, depending on how investigator frame the questions, they can use five different pharmacoeconomic methods–CMA, CEA, CUA, CBA, and CCA to determine the value of a pharmaceutical service or therapy.

REFERENCES

1. Oderda GM. The importance of perspective in pharmacoeconomic analyses. J Pain Palliat Care Pharmacother. 2002;16(4):65-9.

2. Rogers W, Wittink H, Wagner A, et al. Assessing individual outcomes during outpatient multidisciplinary chronic pain treatment by means of an augmented SF-36. Pain Med. 2000;1(1):44-54.

3. Rogers WH. Wittink HM, Ashburn MA, et al. Using the TOPS, an outcomes instrument for interdisciplinary outpatient pain treatment. Pain Med. 2000;1(1): 55-67.

4. Ho M-J, LaFleur J. The Treatment Outcomes of Pain Survey (TOPS): A clinical monitoring and outcomes instrument for chronic pain practice and research. J Pain Palliative Care Pharmacother. 2004;18(2):9-59.

5. hjttp://www.who.int/about/definition/en/ accessed February 15, 2006.

RECEIVED: 11/29/05
REVISED: 02/09/06
ACCEPTED: 02/28/06